I-49 Strategy for recalcitrant MRSA infections – An evolving clinical challenge

P.R. Hsueh*. *Divisions of Clinical Microbiology and Infectious Diseases, Departments of Laboratory Medicine and Internal Medicine, National Taiwan University Hospital, National Taiwan University College of Medicine, Taipei, Taiwan*

Glycopeptides (vancomycin and teicoplanin) represent the gold standard for therapy of invasive infections caused by multidrug-resistant *Staphylococcus aureus*, most notably hospital-acquired methicillin-resistant *S. aureus* (MRSA). Reports of increasing in vitro resistance to glycopeptides combined with reports of clinical failures underscore the need for alternative therapies. Older agents with favorable in vitro potency available in oral and/or intravenous forms include trimethoprim-sulfamethoxazole, rifampin, fusidic acid, fosfomycin, and clindamycin. However, limited clinical data exist to support their routine use as initial therapy in the treatment of invasive disease. Newer treatment options for MRSA include linezolid, quinupristin-dalfopristin, daptomycin, cftobiprole, tigecycline, and nemonoxacin. With the exception of linezolid, these newer agents require intravenous administration. Combination therapy is mandatory for selected invasive diseases refractory to standard monotherapies. These diseases include endocarditis, meningitis, septic arthritis, prosthetic device infections, and other recalcitrant MRSA Infections. Some novel agents are under investigation, consisting of oritavancin, dalbavancin, telavancin, and ceftobiprole. Daptomycin is a promising antibiotic for the treatment of patients with right-sided endocarditis and bacteraemia. However, development of hematogenous spread of MRSA resulting in multiple lung abscesses during daptomycin treatment for bacteremia and right-sided endocarditis and treatment failure for infective endocarditis due to daptomycin-nonsusceptible MRSA have been reported. Routinely tests of the daptomycin susceptibility is necessary before the use as a rescue therapy for persistent MRSA infection and difficult-to-eradicate infectious foci especially after a prolonged glycopeptide therapy. To prevent prolonged glyopeptide therapy, using the maximum tolerated dose of glycopeptide and aggressive adjnctive therapies such as surgical interventions to remove culprit foci are the best strategy for the treatment of recalcitrant MRSA infections.

Concurrent Session 9 – End-Stage Liver Diseases and Complications

I-50 Cirrhotic cardiomyopathy: an unappreciated complication of endstage liver disease

S.S. Lee*. *Liver Unit, University of Calgary, Calgary, Canada*

In patients and animal models with cirrhosis, the heart is abnormal. Although the circulation becomes hyperdynamic, manifested as increased cardiac output and decreased peripheral vascular resistance and arterial pressure, the heart responds subnormally to numerous stimuli/stresses. Cardiac ventricular function under physiological, pharmacological or surgical stress is blunted, with abnormalites of both systolic and diastolic function. This condition is known as cirrhotic cardiomyopathy. Other features of the syndrome include: (a) electrophysiological changes in repolarization including prolonged electrocardiographic QT interval and a curious dissynchrony in the normally tightly-regulated time interval between electrical and mechanical onset of systole, (b) enlargement or hypertrophy of cardiac chambers, (c) markers of cardiac 'distress' such as BNP or pro-BNP and troponin I.

Although these changes when initially described almost 4 decades ago were ascribed to a mild or latent form of alcoholic cardiotoxicity, it is now incontrovertibly established that the condition of cirrhosis per se is associated with this, as patients and animal models with non-alcoholic cirrhosis show the same pattern or cardiac dysfunction. Recent evidence implicates a significant pathogenic role of this syndrome in the development of acute hepatorenal syndrome after spontaneous bacterial peritonitis and poor outcomes such as increased mortality/morbidity after challenges such as TIPS insertion and liver transplantation. It may also explain the uncommon but mysterious and inexplicable onset of heart failure in the peri- and post-transplantation period in patients with no previous history of heart disease or dysfunction.

Several pathogenic mechanisms have been described including: dysfunction or defects in the cardiac β-adrenergic receptor system, plasma membrane physico-chemical milieu (decreased membrane biophysical fluidity due to an increased cholesterol:phospholipid ratio in the plasma membrane lipid bilayer), membrane calcium channels, and humoral factors such as cytokines, nitric oxide, carbon monoxide and endogenous cannabinoids. Many of these pathogenic mechanisms are inter-related and their exact relationship is the subject of ongoing research.

Treatment strategies for cirrhotic cardiomyopathy remain unclear. Fortunately over heart failure is distinctly uncommon. Repolarization abnormalities such as QT prolongation may respond to β-blockade. Promising avenues of inquiry include cardiac anti-fibrogenic therapies such as angiotensin converting enzyme inhibitors. Cirrhotic cardiomyopathy is a previously underappreciated syndrome with important clinical consequences in patients with cirrhosis, especially given the emergence of liver transplantation as effective therapy for endstage liver disease.

I-51 Infectious complications in acute liver failure

V. Bhatia*. *Institute of Liver and Biliary Sciences (ILBS), Delhi, India*

Infection and cerebral edema are the two most common fatal complications of acute liver failure (ALF). ALF is a state of immunosuppression. In addition there are frequent breaches of the skin and mucus membrane barriers, and need for invasive treatments and monitoring. Development of infection at any site during grade I or II encephalopathy (HE) is an independent risk factor for worsening of HE grade. In addition, infection can directly aggravate liver damage, and increases mortality in ALF.

Clinical signs such as high temperature and leukocyte count may be absent in 30% of ALF patients, and daily microbiological surveillance is recommended. An 80% infection rate has been reported from the west. Over 70% of the isolates in the west, were Gram-positive organisms. In our center, the infection rate of ALF patients is around 60% and 80% of our isolates are Gram-negative. The most common isolates are *Acinetobacter baumanni*, *Klebsiella pneumonia, Escherichia coli,* and *Pseudomonas aeruginosa.* We found that 94.7% Gram-negative isolates were ESBL positive, and 66.7% Gram-positive isolates were Methicillin resistant. In addition we had a 12.5% fungemia rate with *Aspergillus spp.* and *tropicalis* and *glabrata* species of Candida being the most common isolates. Western series have reported fungemia rates of